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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/059,521	01/29/2002	Ivan N. Rich	6115-007	5794

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/059,521	RICH, IVAN N.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18-28,31,42-44,57 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18-28,31,42-44,57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 12, 2007 has been entered.

Amendment Entry

2. Applicant's amendment and arguments, filed on February 12, 2007, are acknowledged and have been entered. Claims 1, 5, 19, 20, 23-26, 28, 31, 43, and 44 have been amended. Claims 16 and 17 have been cancelled. Accordingly, claims 1-15, 18-28, 31, 42-44, 57, and 58 are pending and are under examination.

Withdrawn Rejections

3. All rejections not reiterated herein, have been withdrawn.

4. All rejections of claims 15 and 16 are now moot in light of Applicant's cancellation of the claims.

5. In light of Applicant's amendment and arguments, the rejection of claims 1-15, 18-28, 31, 42-44, 57, and 58 under 35 U.S.C. 103(a) as being unpatentable over

Crouch et al. (Journal of Immunological Methods, 160: 81-88 (1993)) in view of Bell et al. (US 2002/0120098 A1) and in further view of Moore et al. (US Patent 5,328,844), is hereby, withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-15, 18-28, 31, 42-44, 57, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (Journal of Immunological Methods, 160: 81-88 (1993)) in view of Bell et al. (US 2002/0120098 A1) and in further view of Bauer et al. (US Patent 6,440,407).

Crouch et al. disclose an assay method for determining the proliferative status (cell proliferation) of a population of primitive (lymphoblastic, promyelocytic) hematopoietic cells. The hematopoietic cells are granulocyte-macrophage colony-forming cells (GM-CFC) and granulocyte colony-forming cells (G-CFC), i.e. TF-1 and NFS-60 cells, isolated from human peripheral blood, and are detected for cytokine dependent proliferation by stimulation of granulocyte-macrophage colony stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) (see Abstract). Other animal cells or tissue tested include those obtained from mammals such as cow (bovine) and mouse (rodent). Initially, the hematopoietic cell lines from peripheral blood

are cultured and maintained in a cell growth culture medium containing 0% to 30% (12.5%) fetal bovine serum (fetal calf serum). Crouch et al. then isolate mononuclear cells (MNCs) from peripheral blood in order to render the MNC sample substantially free of hemoglobin. The MNCs are isolated by Ficoll-Hypaque density gradient centrifugation. In ATP bioluminescence assay, the isolated MNCs are combined with luciferin-luciferase monitoring reagent which generates bioluminescence when contacted with adenosine triphosphate or ATP (see page 81, column 2 and page 82, columns 1 and 2). The amount of luminescence generated by the reagent indicates the amount of ATP present in the MNC cell population, wherein the amount of ATP indicates the proliferative status of the hematopoietic cells.

Crouch et al. differ from the instant invention in failing to teach including methylcellulose and transferrin into the cell growth medium which is maintained in an atmosphere including oxygen. Crouch et al. also does not teach further defining the subpopulations of primitive hematopoietic cells by cell surface markers thereon. Crouch et al. also does not teach using the cells having a proliferative status 1) for transplantation and 2) for testing compound's ability to modulate proliferation of the cells.

Bell et al. disclose stimulation of erythroid progenitor proliferation in cell culture systems. Erythroid progenitor cells are a subset of hematopoietic progenitor cell lineage. The stimulation and proliferation of the hematopoietic stem cells and hematopoietic progenitor cells involve hematopoietic colony-forming cell erythroid macrophage and megakaryocyte stem cells (CFC-GEMM) (see page 4 [0026], page 7

[0071], and page 9 [0085]). Specifically, Bell et al. teach a cell growth medium comprising 30% fetal bovine serum and about 0.4% to about 0.7% (0.8%) methyl cellulose in an atmosphere having between about 3.5% to 7.5% (5%) for use in culturing the hematopoietic cells. The cells are contacted with proliferation agents such as hemoglobin to enhance the growth of erythroid progenitors. The cells are also contacted with other proliferation agents such as cytokine (GM-CSF and Flt3 Ligand) to stimulate nonerythroid hematopoietic progenitor proliferation and to generate a cell population substantially enriched in CFC-GEMM stem cells for use in cell proliferation assay (see page 9 [0084-0087], and Examples 1 and 2). According to Bell et al., erythroid progenitor colony formation is enhanced at lower, more physiological oxygen tensions, such as 5% oxygen (see page 11 [0098-0101]. Bell et al. obtain the cells from bone marrow, cord blood, or peripheral blood. The cells can be cultured and stimulated so as to have adequate proliferative status for transplantation (see page 4 [0030] and page 7 [0078]). Cells may be obtained and enriched from bone marrow, cord blood, fetal liver, or spleen, from mammals including dog, cow, horse, cat, pig, sheep, goat, chicken, primate, or human (see page 8 [0076-0078]). The primitive hematopoietic cells are defined by cell surface markers such as CD34 and glycophorin A present thereon using cell surface marker indicators such as anti-CD34 and anti-glycophorin A and determined using flow cytometry or flow activated cell sorting. The cells can then be isolated by magnetic bead separation, i.e. STEMSEP^{TM} system, or other separation systems, i.e. CEPRATE LC system (see page 12 [0105], page 17 [0144 and 0145] and Example 9). Bell et al. further teach contacting an isolated cell population with a test

compound (Ganciclovir) to determine its ability to modulate, i.e. inhibit, proliferation or differentiate, proliferation of the cell population in comparison to a negative control (see Example 11).

Bauer et al. disclose methods of ex vivo expansion of hematopoietic cells using IL-3 multiple mutation polypeptides. Specifically, Bauer et al. teach culturing hematopoietic cells in a tissue culture medium that is prepared by supplementing Iscove's Modified Dulbecco medium with human transferrin in an amount of 100 ug/ml (0.1 nM) (see column 11, line 53 to column 12, line 66; and especially column 15, lines 36-58). For colony assay evaluation, Bauer et al. also disclose incorporating the cells into an assay culture tube containing Iscove's based methylcellulose, growth factors, and in an atmosphere of 5% oxygen (see column 19, lines 9-22).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the growth culture medium as taught by Bell as modified by Bauer for expanding and stimulating proliferation of progenitor hematopoietic cells and maintaining the cells, so as to be tested for ATP bioluminescence assay as in the method of Crouch in order to determine their proliferative status for treatment and transplantation purposes, because Bell and Bauer specifically taught that their media compositions favor hematopoietic progenitor cell or stem cell growth, expansion, and proliferation upon stimulation, so as to be applicable for transplantation and treatment of patients having hematopoietic disorders, and Crouch's ATP bioluminescence assay provides accurate and safe measure of proliferation status of the cells so as to enable

optimal hematopoietic progenitor cell sample selection and isolation prior to transplantation.

Response to Arguments

7. Applicant's arguments filed on February 12, 2007 have been fully considered but they are not persuasive.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Z4Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
March 15, 2007